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EXAMINER	
SAOUD, CHRISTINE J	
ART UNIT	**PAPER NUMBER**
1647	

DATE MAILED: 03/10/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/928,522	SPURLOCK, MICHAEL E.	
	Examiner	Art Unit	
	Christine J. Saoud	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 December 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *13-30 and 38-49* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13-30 and 38-49* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *See Continuation Sheet*.

Continuation of Attachment(s) 6). Other: copy of 1.131 Dec. from parent app..

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 16 December 2004 has been entered.

Response to Amendment

Claims 13-30 have been amended, claims 31-37 have been canceled and 38-49 have been added as requested in the paper filed 16 December 2004. Claims 13-30 and 38-49 are pending in the instant application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Any objection or rejection of record which is not expressly repeated in this action has been overcome by Applicant's response and withdrawn.

Applicant's arguments filed 16 December 2004 have been fully considered but they are not deemed to be persuasive.

Finality of Previous Office Action

At page 12 of the response filed 16 December 2004, Applicant challenges the finality of the previous Office action. Applicant asserts that the Examiner introduced a new ground of rejection "[w]hen the Examiner argued that an allelic variant is only a naturally-occurring molecule and only a product which occurs in nature" because this is considered "a new basis" for rejecting claims 1-5 under 112/1st paragraph. Applicant's arguments are not persuasive. The grounds of rejection were not changed and the response to Applicant's interpretation of the rejection does not constitute a new ground of rejection, absent evidence to the contrary. See MPEP 706.07(a). Any question as to prematureness of a final rejection should be raised, if at all, while the application is still pending before the primary examiner and is reviewable by petition under 37 CFR 1.181 (See MPEP 1002.02(c)). However, since Applicant has canceled the claims in question and has filed an RCE in the instant application, this argument appears to be moot.

Specification

The disclosure is objected to because of the following informalities:

Page 17 of the specification (bottom of page) contains an address for the ATCC which is out of date. The current address is American Type Culture Collection, 10801 University Boulevard, Manassas, VA 20110-2209. The specification should be brought up to date via an amendment.

Appropriate correction is required.

Claim Objections

Claims 17-18 stand objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim for the reasons of record in the previous Office action(s). Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. The instant claims depend from base claims which have two requirements: 1) the DNA molecule must encode a bovine adipocyte leptin and 2) must hybridize to a specified sequence. The dependent claims 17-18 place size limitations on the DNA of "at least about 20" or "at least about 50" bases, which is no where near the necessary size of a DNA which will encode a bovine leptin polypeptide, absent evidence to the contrary. Therefore, the claims do not appear to further limit the claims from which they depend.

First it should be noted that in response to the above objection, Applicant refers to passages in the published form of the application and to an issued U.S. Patent, of which the instant application is a CIP. Applicant should always include the page and line number of the instant application for basis of claim language and support. The instant application must contain the support for what is being claimed. Additionally, the instant application may differ from these other publications and the Examiner is not examining the other publications, but rather, the instant application.

Applicant argues that "the Examiner's characterization of the 'at least about 20 bases' and the "at least about 50 bases" as a "size limitation" is inaccurate" and that the

Examiner suggests it is improper to define structural features of the isolated DNA in terms of functional attributes. (see page 15 of the response). From Applicant's statements, it is clear that the Examiner and Applicant are not interpreting "encoding bovine leptin polypeptide" as the same thing. (See new ground of rejection for indefiniteness below).

The specification is directed to "DNA and RNA molecules and their respective allelic variants that encode a bovine adipocyte polypeptide, termed "leptin," or a functional derivative thereof, and the bovine leptin protein itself, or a functional derivative thereof" (page 5 of the specification). This language is being interpreted as "leptin" being the full-length molecule having the amino acid sequence of SEQ ID NO:4. Therefore, reference to a molecule "which encodes a bovine adipocyte polypeptide leptin" would mean that the molecule would encode a protein that would be considered leptin from cows. A fragment of 8 amino acids, while described in the instant specification and supported by the instant specification, is not "leptin"; it is a fragment of leptin. This characterization is supported by Applicant's own specification which states

> The polypeptide of this invention has an amino acid sequence as depicted in Figures 1 and 3-5. Also intended within the scope of the present invention is any polypeptide having at least about 8 amino acids present in the above-mentioned sequence. (page 6 of the specification) .... As alternatives to a native purified or recombinant bovine adipocyte polypeptide molecule, functional derivatives of the bovine adipocyte polypeptide may be used. As used herein, the term "functional derivative" refers to any "fragment", "variant", "analog", or "chemical derivative" of the bovine adipocyte polypeptide ...(page 7 of the specification) ... A "fragment" of the bovine adipocyte polypeptide as used herein refers to any subset of the molecule, that is, a shorter polypeptide. (page 7 of the specification)

The fact that the base claim requires the isolated DNA molecule to encode "leptin" means that it must be of sufficient length to encode a protein that would be of sufficient length to be considered "leptin". The fact that the specification separately defines a "fragment" from the molecule which is called "bovine adipocyte polypeptide" further supports this interpretation of "bovine adipocyte polypeptide leptin" as being the polypeptide of SEQ ID NO:4.

Applicant argues that a person of ordinary skill in the art would know how to use the invention being claimed, however, because this is an objection to the claims for failure to limit, these arguments are not relevant. Applicant additionally argues that use of the term "at least" is not intended to limit the isolated DNA to only those 20 to 50 bases in length. The Examiner did not suggest that the claims were limited to that length, but rather that the claims are directed to embodiments which encompass molecules of this length. And since molecules of this length do not encode "bovine adipocyte polypeptide leptin" as interpreted by the Examiner and supported by Applicant's own disclosure, the instant claims do not further limit the claim from which they depend. Molecules of this length would encode a fragment, and claims of this nature could be presented as independent claims or they could be presented in a different manner so as to not include the requirement that they encode "bovine adipocyte polypeptide leptin".

The objection to the claims is maintained. (Applicant misstated that a rejection was made based on 37 CFR 1.75(c) – see basis for **objection** above.)

Claims 38-42, 44, 46 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. The recited claims and the claims from which they depend all recite language regarding encoding "bovine adipocyte polypeptide leptin" or "bovine leptin polypeptide". However, the instant specification only describes a single protein of leptin which has been isolated from cows, making it bovine leptin (SEQ ID NO:4). Specifically, the specification indicates at page 2 "this invention is directed to a bovine adipocyte polypeptide (i.e., the bovine leptin protein)" and uses the terms "bovine adipocyte polypeptide" and "bovine leptin" interchangeably as meaning the same protein throughout the specification (see page 5 for example). Therefore, the further dependent claims which recite that the encoded protein is "bovine leptin" is not further limiting.

Applicant should be advised that these claims could be objected to under 37 CFR 1.75 as being substantial duplicates of the base claims if the base claims are found allowable. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). Since the base claims are not allowable at this time, the objection is not being made.

Claim Rejections - 35 USC § 112

Applicant argues at page 17 of the response that claims 1-5 are allowable. This argument is moot in light of Applicant's cancellation of the claims. If the claims are reinstated, they will be rejected. Applicant argues that the 112/1st paragraph rejection based on "allelic variant" is moot in light of the cancellation of this language from the claims. The rejection is being withdrawn in light of the absence of the language from the claims, however, any argument that the claims are directed to "allelic variants" or reinstatement of the language will be cause for rejection of the claims based on lack of written description of this subject matter for the reasons of record in the previous Office action(s). However, a new ground of rejection for lack of written description is being added in light of review of the prosecution history of the parent application.

Claims 13-30 and 38-49 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The instant claims are generically directed to isolated DNA and RNA which encode bovine leptin, wherein the nucleic acid molecule hybridizes to a nucleic acid sequence of SEQ ID NO:3 (or a variant thereof) under stringent hybridization conditions. However, the only such molecule disclosed in the instant specification is the nucleic acid molecule of SEQ ID NO:3 which encodes the protein of SEQ ID NO:4.

In the parent application (08/688,908), to which the instant application claims priority, the inventor, Michael E. Spurlock, filed a Declaration under 37 C.F.R. 1.132

regarding isolation of the leptin gene using murine or human leptin as a probe. However, the comments made regarding using a murine or human sequence as a probe are also applicable to using a bovine sequence to isolate other related intraspecies molecules. At paragraph 5 of the Declaration, Dr. Spurlock states "Intraspecies homology also presents an obscuring factor in isolating a particular gene in one species using primers derived fro ma different species. Specifically, multiple genes in the target species may each have similarly high homology to the same primers based on a known gene of another species ... Separating and purifying highly homologous intraspecies genes is difficult with the difficulty increasing as the homology increases. At paragraph 6 of the Declaration, Dr. Spurlock states "The bottom line is that you do not know the bovine leptin sequence until you have the bovine leptin sequence. Even then, you may have variations within the species because of the genetic diversity that exists within all species populations. Some of these variations may be very important relative to the functionality of the protein".

Based on these statements by Applicant, it is clear that one of ordinary skill in the art would not know bovine leptin until they had bovine leptin. The only bovine leptin described in the instant specification is the protein of SEQ ID NO:4, and the only nucleic acid encoding bovine leptin is that of SEQ ID NO:3. To provide evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of compete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product,

or any combination thereof. In this case, the only factor present in the claim is a partial structure in the form of a recitation of hybridization ability. There is not even identification of any particular portion of the structure that must be conserved. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to

be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only isolated polynucleotide of SEQ ID NO:3, or encoding the amino acid sequence of SEQ ID NO:4, but not the full breadth of the claims meets the written description provision of 35 U.S.C. § 112, first paragraph. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

The rejections based on 112/2nd paragraph will be addressed first because interpretation of the claims is important for why the claims are rejected under 112/1st paragraph.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 19-30 and 38-49 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 13, 24, 25, 27, 28, 29, 30, 43, 45, recite the article "a" or "an" in place of "the" when referring to the sequence represented by a sequence identifier. This is indefinite when referring to a single sequence because reference to a specific sequence would require the use of the article "the". The use of "a" implies that there are multiple sequences to chose from or represented by the sequence identifier, which is not the

case when referring to a specific sequence as one is when referencing a sequence identifier.

Claims 14, 15, 17-20 are indefinite for the recitation "at least about" in conjunction with a number of nucleotides which are to hybridize. This recitation is indefinite because the lower limits of what are to be encompassed by the claims is not clear. The instant specification does not indicate what range "at least about" is meant to encompass. Furthermore, "at least" is in direct conflict with "about" since "at least" sets a lower limit to the range, but "about" changes that limit. Therefore, the claims are indefinite because the metes and bounds of "at least about" cannot be determined.

Claims 13-30 and 38-49 are indefinite for the use of "bovine adipocyte polypeptide leptin" or "bovine leptin polypeptide" (dependent claims are included as well, even if they do not explicitly recite the noted language). These recitations are used separately as well as in conjunction with one another as if to denote a distinction between the molecules which are encoded. However, a fair reading of the instant specification would indicate that the above recitations all refer to the same protein, which is leptin produced in cows. Only a single protein is disclosed in the instant specification (SEQ ID NO:4) and there is no disclosure to distinguish one recitation from another. Therefore, the use of these recitations as limitations in the claims is vague and indefinite because the specification discloses that they are the same protein as evidenced by the disclosure at page 5. The metes and bounds of what is being claimed cannot be determined because no differences can be ascertained for the different recitations which appear to mean the same thing.

Claims 13-30 and 38-49 are indefinite for the limitation of "stringent hybridization conditions". The limitation "stringent hybridization conditions" is equivalent to reciting a range without indicating the metes and bounds of the conditions since there is no indication of what conditions are to be encompassed by the claims. The specification does not provide a definition of what conditions are considered "stringent" and the art recognizes a multitude of conditions which could be used and considered "stringent". Page 8 of the specification makes reference to hybridization that "[I]n order to achieve higher specificity of hybridization, characterized by the absence of hybridization to sequences other than those encoding the polypeptide or a functional derivative thereof, a length of at least about 50 nucleotides is preferred". Based on this language, it would seem that claims that include the limitation of "at least about 20 nucleotides" would be in direct conflict with the limitation that "stringent hybridization conditions" are used. Hybridization conditions are found in the specification in conjunction with Example II, however, the specification does not disclose that these conditions are what is intended by the recitation of "stringent hybridization conditions".

Applicant argues this rejection beginning at page 24 through page 46 of the response. The Declaration under 37 CFR 1.132 filed 16ecember 2004 is insufficient to overcome the rejection of claims 13-30 and 38-49 based upon indefiniteness as set forth in the last Office action (as applied to the previous filed claims) because: the Declaration and the arguments which accompany it demonstrate that there are a multitude of conditions which the prior art and those skilled in the art recognize as being "stringent hybridization conditions". Varying the length of the probe, the temperature at

which the hybridization occurs, the salt concentration at various stages including wash steps and varying denaturing agents can all provide different specificities in hybridization. Without knowing which conditions are intended by the claims, the metes and bounds of those molecules which are encompassed by the claims cannot be determined.

Applicant makes many references to the conditions in Examples II and III of the specificatino, however, limitations from the specification cannot be read into the claims. Applicant may wish to include the conditions which are exemplified in Examples II and III into the claims in order to avoid the rejection of record. However, in the absence of a true definition in the specification that indicates what conditions are intended by "stringent", the rejection is maintained as it is clearly supported by Applicant's own arguments and the Declaration filed that there are a number of variables involved in hybridization, and therefore, a number of different conditions which would provide for "stringent" hybridization.

Claims 16, 21, 23, 24, 26, 28, 29 are directed to nucleic acid molecules (DNA, mRNA) which "hybridizes" to "substantially all" of the bases of a recited sequence. However, these claims are indefinite for the failure to indicate what is intended by the recitation "substantially all".

Applicant argues at pages 24-28 that those skilled in the art will be able to understand with a reasonable degree of accuracy what subject matter is circumscribed by the invention, and therefore, that the recitation "substantially all" is definite. Applicant

further argues that the Examiner has issued a patent which includes the recitation "substantially all" as well as citing case law related to indefiniteness.

With regard to patents issued by the Examiner with "substantially all" language; each application is examined on its own merits. The facts surrounding the issued patent are not the same and are not applicable to the instant application. In the instant application, the claims are attempting to define the structure of the isolated nucleic acid molecule by its ability to hybridize to another nucleic acid molecule. Hybridization conditions are influenced by a number of different factors, including probe length. The longer the probe length and how many bases hybridize to the probe, influences what type of molecules are being isolated. As is pointed out elsewhere in this action, "stringent hybridization conditions" are considered indefinite without more because there are a number of conditions which could be considered "stringent" and dependent on which conditions are used, different nucleic acid molecules will be isolated. Likewise, depending on how many bases hybridize (anywhere between 50% and 100% based on Applicant's explanation at page 33), different types of molecules will be encompassed by the claims, as well as different stringency conditions. The specification does not define "substantially all" and its use in conjunction with the indefinite "stringent hybridization conditions" clearly does not provide sufficient explanation of the metes and bounds of the claims.

If the claims are amended to include those conditions which are to be considered "stringent" and are limited to those conditions provided in the instant specification, then the use of the recitation "substantially all" may be definite in that context. However, as

the claims are currently written, the metes and bounds of what is being claimed is indefinite.

Claims 13-30, 38-49 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The first step in determining if a claim meets the enablement requirements of 35 U.S.C. 112, first paragraph, is understanding what is being claimed. The instant claims are directed to nucleic acid molecules which encode a bovine leptin polypeptide, wherein the nucleic acid hybridizes to at least about 20-50 bases of SEQ ID NO:3, or wherein the nucleic acid molecule is at least 20-50 bases long. It is clear that the instant specification encompasses and intends for fragments of bovine leptin to be encompassed in the scope of the invention. However, the instant specification only describes a single protein which can be called "bovine adipocyte polypeptide leptin" or "bovine leptin polypeptide", and this protein is 146 amino acids in length. The prior art nucleic acid molecules which encode leptin are also described in Figures 3A-3B, which encode a leptin of a similar length to that of the disclosed bovine leptin. The specification distinguishes fragments from the "leptin" depicted in SEQ ID NO:4 at page 6 of the specification; "[a]lso intended within the scope of the present invention is any polypeptide having at least about 8 amino acids present in the above-mentioned

sequence." Therefore, the claims are directed to nucleic acid molecules which encode bovine leptin (functional limitation) wherein the nucleic acid molecule hybridizes to at least about 20 (or 50) nucleotides of a disclosed nucleic acid molecule or wherein the isolated nucleic acid molecule is at least about 20 (or 50) bases in length (structural limitation).

First, the art does not recognize a nucleic acid as short as 20-50 nucleotides long that encodes a leptin molecule and the instant specification fails to teach a molecule meeting this limitation. The specification does teach that a fragment of 20 nucleotides is intended in the scope of the claims, but it does not teach that this length is sufficient for encoding leptin as defined in the instant specification as corresponding to SEQ ID NO:4. Therefore, one of ordinary skill in the art would not find such a length sufficient for encoding a leptin molecule from cows, absent evidence to the contrary, and the claims are not enabled for such. The structure which is given is not sufficient to result in the required function of the claims, and the claims are not enabled.

Applicant argues the rejection in the response. However, Applicant's arguments are based on the premise that a nucleic acid molecule of "at least about" 20 bases encodes bovine leptin. For the reasons given above and supported by the disclosure of the instant specification, this is a false premise. Therefore, the rejection is maintained for the reasons of record and for those reasons given above. Applicant may wish to amend the claims to eliminate the functional requirement that the isolated nucleic acid molecule encode bovine leptin, and this may obviate this ground of rejection.

Claim Rejections - 35 USC § 102

Claims 25-30, 41-42, 45-49 are rejected under 35 U.S.C. 102(a) as being anticipated by TELLAM et al. (Genbank Acc. No. U43943, Bos Taurus OBESE mRNA, 27 January 1996) for the reasons of record in the previous Office action(s).

Applicant asserts that the Declaration under 37 CFR 1.131 is sufficient to overcome the instant rejection. MPEP 715.03(b) states that proof of prior completion of a species different from the species of the reference will be sufficient to overcome a reference indirectly under 37 CFR 1.131 if the species shown in the reference would have been obvious in view of the species shown to have been made by the application. However, the species in the reference would not have been obvious in view of the species in the instant application, absent evidence to the contrary and in view of current case law governing biotech applications. Alternatively, the applicant may be able to antedate the reference indirectly by, for example, showing prior completion of one or more species which put him or her in possession of the claimed genus prior to the reference's date. Applicant has not successfully done this for a number of reasons.

Applicant first argues that the Examiner did not give sufficient explanation of why the first Declaration was insufficient to overcome the rejection based on TELLAM et al. First, the relationship of the different Exhibits does not make sense. The sequence alignments of Exhibits D and E appear to be with the nucleic acid molecule of the instant application. The sequence of Exhibit C cannot be determined because the copy is so poor; the left hand portion is unreadable. Lastly, the correspondence of the "450 base pair clone" to the nucleic acid sequence of the instant application is in question. It

is not clear if the nucleic acid molecule of this clone would hybridize to the nucleic acid molecule of SEQ ID NO:3. Applicant is invited to provide a clear line of explanation as to the sequence of this clone (i.e. a clear copy of the nucleic acid sequence with an indication of the orientation of the molecule) as well as evidence, possibly sequence alignment, which shows that it is within the claimed genus. In the Declaration filed 16 December 2004, paragraph H attempts to relate the sequence of the clone (450 bp clone) to the nucleic acid molecule of SEQ ID NO:3 of the instant application. However, the Examiner cannot make the sequence line up as asserted, and the arguments presented do not make sense in the context of sequences which do not align. Therefore, the Declaration is not sufficient to overcome the rejection based on this reference.

At page 47 of the response, Applicant argues that claims 23-30 are not genus claims and asserts that the Examiner does not provide rationale, support or basis for this characterization of the claims. Applicant should refer to MPEP 806.04(d) which provides the definition of a generic claim. The Examiner cannot use 715.03(A) to evaluate the evidence because the claims are not directed to a species (i.e. single, molecular embodiment); the claims clearly encompass more than a single molecule. The Examiner cannot use 715.03(C) to evaluate the evidence because the claims are not directed to embodiments – but rather a generic molecule defined by some amount of structure and function. Furthermore, regardless of which portion of the MPEP is being used to evaluate the evidence, the evidence is not sufficient to overcome the

rejection because the evidence is incomplete and confusing and no conclusions can be drawn from the evidence which has been provided.

At page 49 of the response Applicant asserts that the 450 bp clone is a "functional derivative, functional variant, or variant", however, there is no evidence that the nucleic acid molecule of the Declaration has any biological activity at all, and therefore, cannot be assumed to be a "functional" molecule. Applicant is again referred to the Declaration of Dr. Spurlock which was submitted in the parent application (08/688,908) which indicates that "you may have variations within the species because of the genetic diversity that exists within all species populations. Some of these variations may be very important relative to the functionality of the protein". Regardless, since the submitted evidence was not sufficient to overcome the rejection of record, the asserted functionality of the 450 bp clone is moot for the time being.

Claim Rejections - 35 USC § 103

Claims 13-24, 38-40, 43-44 are rejected under 35 U.S.C. 103(a) as being unpatentable over TELLAM et al. (Genbank Acc. No. U43943, Bos Taurus OBESE mRNA, 27 January 1996) for the reasons of record in the previous Office action(s).

Applicant asserts that the Declaration filed under 1.131 obviates the instant rejection. This argument is not persuasive and the Declaration(s) is ineffective for the reasons provide above. Therefore, the rejection is maintained.

Claims 21-30 and 38-49 are rejected under 35 U.S.C. 103(a) as being unpatentable over Friedman et al. (U.S. Pat. No. 6,309,853) for the reasons of record in the previous Office action(s) as applied to the previous filed claims.

The instant specification defines a functional derivative as

> Any "fragment", "variant", "analog", or "chemical derivative" of the bovine adipocyte polypeptide that retains at least a portion of the function of the bovine adipocyte polypeptide which permits its utility in accordance with the present invention. (page 7 of the specification)

The instant claims are directed to isolated nucleic acids which encode bovine leptin or a "functional derivative thereof" or "variant thereof" . The prior art of Friedman et al. (U.S. Pat. No. 6,309,853) disclose nucleic acids which encode human and mouse leptin, which would be considered functional derivatives and/or variants of the disclosed bovine leptin since they encode leptin molecules and would possess similar functional properties as those of the bovine leptin, absent evidence to the contrary. Friedman et al. teach that the leptin gene (or OB) could be isolated from domestic animals using the methods disclosed therein (see column 26, line 53 to column 27, line 49). Friedman et al. specifically mention cows as a domestic animal for which leptin would be useful (see column 48, lines 41-57). Friedman et al. do not specifically disclose an isolated nucleic acid encoding a bovine leptin polypeptide. However, it would have been obvious to use the nucleic acid of Friedman et al. encoding human or mouse leptin and hybridize it to a bovine cDNA library and isolate a nucleic acid molecule encoding porcine leptin because Friedman et al. teach methods for isolating leptin encoding nucleic acids and also teach that it would be beneficial to administer leptin to cows. It would also have

been prima facie obvious to use the nucleic acid of Friedman et al. encoding human or mouse leptin and hybridize it to bovine genomic DNA to isolate the gene encoding bovine leptin because it would have been beneficial to more completely understand the gene structure of bovine leptin. It also would have been prima facie obvious to use the nucleic acid of Friedman et al. encoding human or mouse leptin and hybridize it to bovine mRNA to isolate the mRNA encoding porcine leptin for the benefit of understanding the nature of bovine leptin expression. Therefore, the invention as a whole would have been obvious at the time it was made, absent evidence to the contrary.

Applicant should note that the instant rejection is being made because the claims do not require the specifics of the bovine leptin of the instant specification, and therefore, methods of isolating nucleic acids for leptin using a functional equivalent of bovine leptin encoding DNA encompasses methods using human or murine DNA encoding leptin.

Applicant argues the rejection at pages 58-64 of the response. Applicant's arguments appear to be based on the premise that the bovine leptin of the instant application is functionally different from the human and mouse leptin of the prior art. However, the rejection is not one of anticipation, but rather that the human and mouse leptin of the prior art meet the limitation of being functional derivatives based on the disclosure of the instant specification. Because Friedman et al. teach nucleic acid molecules which are "functional derivatives" and "derivatives" of the bovine leptin of the instant application and because Friedman et al. teach that the nucleic acid molecules

encoding leptin could be used to isolate nucleic acid molecules encoding leptin from other species, specifically cows, isolated nucleic acid molecules encoding bovine leptin are obvious over the teachings of Friedman et al.

Applicant refers to the Declaration submitted with the response as evidence that human and mouse leptin do not have the exact same activity as bovine leptin, and therefore, are not functional derivatives. However, Applicant is reading limitations into the claims which are not present in the specification as filed or supported by the instant specification as filed. The instant specification only requires retention of "at least a portion of the function of the bovine adipocyte polypeptide", which could mean that the polypeptide only retain antigenicity, for example. Applicant's reliance on the very detailed biological differences between bovine leptin and human/mouse leptin is noted, but is not persuasive to obviate the rejection for the reasons provided above.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christine J. Saoud whose telephone number is 571-272-0891. The examiner can normally be reached on mttr, 8:00-2:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on 571-272-0961. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

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